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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/518,081	03/03/2000	Leland Shapiro	SHAP-000300	5429

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EXAMINER	
MOORE, WILLIAM W	
ART UNIT	PAPER NUMBER
1656	
MAIL DATE	DELIVERY MODE
09/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/518,081	SHAPIRO, LELAND	
	Examiner	Art Unit	
	WILLIAM W. MOORE	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 31 May 2008 has been entered.

Response to Amendments

The Response filed 31 May 2008 cancels claims 1-32 and presents the new claims 33-43, all of which are drawn to methods requiring administration of the elected α1-antitrypsin inhibitor, "AAT" hereinafter. The claim amendments overcome the objection of record of claim 1 and the rejection of record of claims 1, 3, 4, 7, 10, 12-17, and 30 herein under the second paragraph of 35 U.S.C. § 112, which objection and rejection are WITHDRAWN. This communication is not made final because new grounds of rejection, including a provisional rejection for nonstatutory obviousness-type double patenting based on claims of the recently-filed US application serial No. 12/051,373, are stated hereinbelow.

Claim Objections

Claims 33 and 43 are objected to because of the following informalities: In both of claims 33 and 43 the second occurrence of the term "variant" is improperly recited in the plural. Appropriate correction is required, e.g., amending both claims to delete the word "variants" and replace it with the word "variant".

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 33-43 are provisionally rejected, essentially for reasons of record, on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 7-11, and 34-36 of copending Application No. 10/427,929. Although the conflicting claims are not identical, they are not patentably distinct from each other because a method of inhibiting apoptosis in a subject by administering α1-antitrypsin when the subject suffers from any of arthritis, Alzheimer's disease, autoimmune disease, myocardial infarction, stroke, and ischemia-reperfusion injury of the claims pending herein is also a method of treating an animal suffering from induced inflammation by administering "α1-antitrypsin or a peptide derivative thereof" of the copending claims because arthritis, autoimmune disease, myocardial infarction, stroke, and ischemia-reperfusion injury are all well-known to induce inflammation and a preferred agent for administration in methods of all of the copending claims is α1-antitrypsin. This is a provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented

Claims 33-43 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 29-46 of the new, copending, Application No. 12/051,373. This is a new ground of rejection because claims of the copending application have recently been filed. Although the conflicting claims are not identical, they are not patentably distinct from each other because a method of inhibiting apoptosis in a subject by administering α1-antitrypsin when the subject suffers from autoimmune disease of the claims pending herein is also a method of treating Type 1 diabetes, an autoimmune disease, by administering "α1-antitrypsin or derivative thereof" of the copending claims. This is a provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

While Applicant's requests at page 4 of the Response filed 31 May 2008 that the issue of nonstatutory obviousness-type double patenting be deferred until an indication of allowable subject matter occurs, the rejections of record must be maintained until and unless a Terminal Disclaimer is filed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33-43 are rejected, essentially for reasons of record, under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The subject matter described by the new claims 33-43 does not differ from claims 1 and 3, now combined as claim 33 herein, 4, 7, 10, 12, 14-16, 31, and 32 rejected in the communication mailed 30 November 2007. Applicant's arguments at page 4 of the Response filed 31 May 2008 have been fully considered but are not persuasive. Applicant suggests that identification of disease conditions wherein apoptosis occurs, e.g., at page 4, lines 10-21, might indicate that administering α1-antitrypsin [AAT] may inhibit apoptosis and also suggests that the specification "clearly shows that AAT inhibits apoptosis", concluding that "by administering AAT one can inhibit apoptosis". Claims 33-43 are drawn to a method of inhibiting apoptosis "in a subject" that must be, at least, a vertebrate and must be suffering from at least one among a set of diseases of medical conditions. The issues presented with regard to written disclosure are (i) whether the elected AAT is shown to inhibit the process of apoptosis, which exploits many cellular pathways, all intracellular, while affecting or ameliorating the diverse medical conditions recited in claims 33 and 43 and (ii) whether there is a disclosure of a method of administering a "therapeutically effective amount" of AAT that inhibits of apoptosis in "a subject . . . suffer[ing] from" one of the diverse medical conditions. The specification proposes administering AAT to rats upon surgical induction of myocardial infarction or stroke in sections 6.1 and 6.7 at pages 15, 16, and 18 but fails to demonstrate that administration of AAT at any particular time before, during, or after such a surgical procedure has any protective affect on the heart muscle or nervous system of a living animal. The specification also proposes, but again does not show, that treatment of donor organs with AAT might reduce ischemia during transport in section 6.6 at page 18. The only suggestion in the specification that AAT has an affect on apoptosis does not involve its administration to an intact animal. The *in vitro* apoptosis assays conducted with neuronal cells in culture, see section 6.5 and Figure 2, provide no basis for concluding that the contrasting results of serum depletion and presence of absence of AAT in cell culture have a predictable relationship to protection of neurons in an intact animal in view of the modes of administration

recited in, e.g., claim 40. The issue of enablement - whether or not the specification provides guidance for administering a serine protease inhibitor to a subject adequate for a therapeutic affect by inhibiting apoptosis - is addressed in the following rejection.

The specification fails to exemplify or describe the practice of methods of claims 33-43 wherein administering AAT to an intact animal that suffers any of the recited medical conditions has any affect on the intracellular pathways of apoptosis, acknowledged in the discussion at pages 3 and 4 of the specification, by inhibiting surface or intracellular proteases to inhibit apoptosis. The specification proposes no proteases that AAT might affect other than caspases, granzymes, and cathepsins, all of which are intracellular or organelle-resident proteases. The specification fails to disclose any method of administration of AAT to a subject that delivers AAT to the cytosolic or nuclear compartments of any mammalian cell that may undergo apoptosis in tissues wherein the medical conditions recited in claim 1 transpire, e.g., neurons, epithelial cells, muscle cells, or connective tissue cells. The specification does not show that administering AAT may otherwise affect or ameliorate stroke, arthritis, muscular dystrophy, multiple sclerosis, arteriosclerosis, autoimmune disease, ischemia-reperfusion injury, neurodegenerative disease, or myocardial infarction and establishes no nexus between the ability of AAT to inhibit certain serine proteases and the contribution of serine proteases to these diseases or medical conditions. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. § 112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The specification furnishes no relevant identifying characteristics of cell-surface or extracellular serine proteases, or any other kind of proteases, that might be a target of AAT when administered to a living animal via its circulatory system, or administered directly to a tissue or cavity, e.g., orally, transdermally, intracerebroventricularly, by inhalation, epidurally, or intramuscularly, and might result in inhibition of apoptosis, a process mediated by intracellular proteolytic activity. Neither does the specification disclose a method of administration that might result in inhibiting apoptosis as well as affecting any of the medical conditions recited in claim 1. The rejection of record is therefore sustained.

Claims 33-43 are rejected, essentially for reasons of record, under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably provide enablement for a method of inhibiting apoptosis mediated by the proteases disclosed in the specification to initiate apoptosis, i.e., caspases, granzymes, and cathepsins, using a serine protease inhibitor to which the cells in tissues affected by the medical conditions recited in claims 33 and 43 are impermeable. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice a method of the invention commensurate in scope with these claims.

The subject matter described by the new claims 33-43 does not differ from claims 1 and 3, now combined as claim 33 herein, 4, 7, 10, 12, 14-16, 31, and 32 rejected in the communication mailed 30 November 2007. Applicant's arguments at page 4 of the Response filed 31 May 2008, apparently intended to address both rejections of record herein under the first paragraph of 35 U.S.C. § 112, have been fully considered but are not persuasive. Applicant suggests that identification of disease conditions wherein apoptosis occurs, e.g., at page 4, lines 10-21, might indicate that administering α1-antitrypsin [AAT] may inhibit apoptosis and also suggests that the specification "clearly shows that AAT inhibits apoptosis", concluding that "by administering AAT one can inhibit apoptosis". As noted in the communication mailed 30 November 2007, the specification does not teach, and the prior art of record herein does not disclose, how to introduce an α1-antitrypsin inhibitor within the cytosolic and nuclear compartments of nervous, muscular, epithelial, or connective tissue cells, i.e., the particular cellular compartments wherein caspases, granzymes, and cathepsins are known to mediate the process of apoptosis, either by the route of administration proposed in the hypothetical of section 6.1 of the specification, by any route of administration of claim 40, any other route of administration. The specification nowhere suggests how to deliver α1-antitrypsin inhibitor to cytosolic or nuclear compartments of cells of nervous, muscular, epithelial, or connective tissues in order that it might interact with caspases, granzymes, or cathepsins, and the prior art of record also lacks such a suggestion. To the extent the prior art has been applied to the claimed subject matter during the course of prosecution of this application, it has addressed the set of intended medical results of a claimed method, results which need not be mediated by the process of apoptosis, but could be mediated by administration of AAT to affect a non-cellular, or an extracellular, process. The rejection of record is therefore sustained.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr Bragdon, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general

nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

/Nashaat T. Nashed/
Nashaat T. Nashed, Ph.D.
Supervisory Primary Examiner
Art Unit 1656

William W. Moore
18 August 2007